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The Multifaceted Chemistry of Variously Substituted α,β-Unsaturated Fischer Metalcarbenes

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Abstract The insertion of an alkyne into an α,β-unsaturated Fischer metalcarbene complex leads to a 1-metalla-1,3,5-hexatriene. This usually undergoes subsequent insertion of a carbon monoxide molecule, and the resulting dienylketene complex, in a 6π-electrocyclization, yields an alkoxycyclohexadienone or its tautomeric hydroquinone monoether. The overall process is a [3+2+1] cocyclization and constitutes the so-called Dötz reaction. With a dialkylamino instead of the alkoxy group on the carbene center, or an additional dialkylamino group on C3 of an alkoxycarbene complex, the 1-metalla-1,3,5-hexatrienes resulting from alkyne insertion more generally do not undergo CO insertion, but direct 6π-electrocycliza-

tion and subsequent reductive elimination to yield five- rather than six-membered rings. 1-Dialkylamino-1-arylcarbenemetals thus yield indenes, and 1-alkoxy-3-dialkylaminopropenylidenemetal complexes with alkynes furnish 3-alkoxy-5-dialkylaminocyclopentadienes, which essentially are protected cyclopentenones and even doubly protected cyclopentadienones. The multifunctionality of these cyclopentadienes makes them highly versatile building blocks for organic synthesis. Synthetically useful cyclopentenones are also obtained from 1-cyclopropyl-1-alkoxycarbenemetals with alkynes. Yet, with certain combinations of substituents and conditions, the amino-substituted metallatrienes can also undergo CO insertion with subsequent cyclization to five-membered rings, twofold alkyne and CO insertion with subsequent intramolecular [4+2] cycloaddition to yield cyclopenta[*b*]pyranes, or even threefold alkyne insertion with subsequent twofold cyclization to yield spiro[4.4]nonatrienes. Variously amino-substituted α,β-unsaturated Fischer carbenes can also give rise to pyrrolidines, pyridines, and pyrroles. Normal, i.e., 1-alkoxy-substituted, α,β-unsaturated Fischer carbene complexes react with acceptor-substituted alkenes and alkadienes to yield donor–acceptor-substituted vinylcyclopropanes or cyclopentenes and cycloheptadienes, respectively. Enantiocontrolled formal [3+2] cycloadditions of chirally modified alkoxycarbenemetals with imines can be achieved to yield, after hydrolysis of the alkoxypyrrolines, 1,2,5-trisubstituted pyrrolidin-3-ones with high enantiomeric excesses.

Keywords Fischer carbenes · Template synthesis · Cocyclization · Cycloaddition · Cyclopentadienes · Cyclopentenones · Domino reactions

1 Introduction

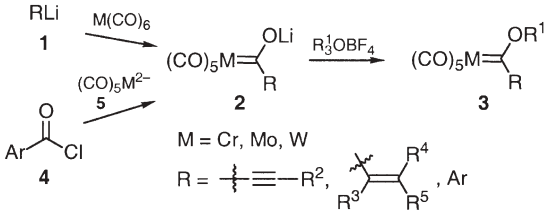
When E. O. Fischer et al. discovered the straightforward access to alkoxycarbene complexes of chromium and other transition metals about four decades ago [1], it was not obvious that they would soon start to become an important item in the toolbox for organometallics and organic synthesis [2, 3]. One of the most important features of Fischer carbene complexes is the distinctly electron-deficient nature of the carbene carbon due to the strong electron-withdrawing effect of the pentacarbonylmetal fragment. It makes such a carbon atom more electrophilic than the carbon atom of any carbonyl group and, as a consequence, an alkenyl or an alkynyl moiety in an α,β-unsaturated Fischer carbene complex is more active toward any sort of nucleophile than the carbonyl carbon atom in a corresponding ester, amide, and/or thioester [4]. As electrophilic species, such α,β-unsaturated Fischer carbene complexes, unlike carbonyl compounds, readily undergo insertion with alkynes, and in certain cases even alkenes, to furnish reactive intermediates from which a large variety of different products can be formed [5, 6]. In particular, the formal [3+2+1] cycloaddition of an α,β-unsaturated (or an α-aryl-substituted) Fischer carbene complex, an alkyne, and a carbon monoxide molecule to form a six-membered ring – the so-called Dötz reaction – has convincingly been applied toward the preparation of a large variety of natural products and other interesting molecules (see Chap. 4 in this book) [7–9]. Yet, a number of α,β-unsaturated Fischer carbene

complexes, especially β-amino-substituted ones, follow different reaction pathways to yield five-membered carbo- and heterocycles without or with carbon monoxide insertion, as well as more complex bicyclic, spirocyclic, and tricyclic structures. In view of all the different reaction modes accessible to them, α,β-unsaturated Fischer carbene complexes can be regarded as true chemical multitalents [10, 11].

2
Synthesis of α,β-Unsaturated Fischer Carbene Complexes

2.1
From (Pentacarbonyl)metallaacylates

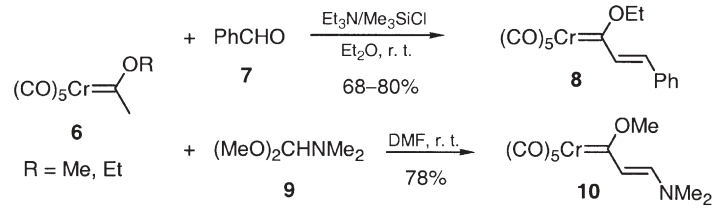
α,β-Unsaturated Fischer carbene complexes **3** are prepared from lithiated alkynes (or alkenes, arenes) **1** according to a variant of the classical route of Fischer et al. (Scheme 1) [12–14]. Treatment of **1** with hexacarbonylmetals affords a (pentacarbonyl)metallaacylate **2**, which can be trapped with hard alkylating agents (especially Meerwein salts) to form stable Fischer carbene complexes **3**. The key intermediates **2** are also accessible from acid chlorides **4** and pentacarbonylmetallates **5** [15].



Scheme 1 Synthesis of α,β-unsaturated Fischer carbene complexes **3** from (pentacarbonyl)-metallaacylates **2** [12–15]

2.2
From Alkyl-Substituted Fischer Carbene Complexes

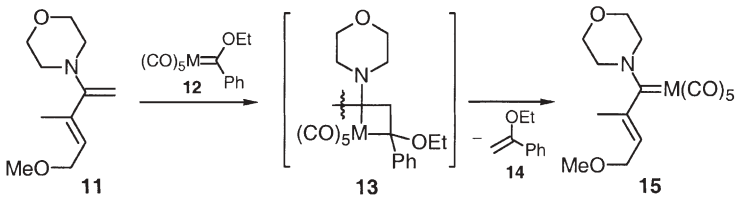
Due to the high α-C,H acidity in the alkoxyethylidene complexes **6** (e.g., pK_a=8 (R=Me)) [16], transformations via an enolate analog are possible and have been used to introduce additional functionality into the carbene side chain to access various Fischer carbene complexes [3]. The α,β-unsaturated complex **8** could be obtained from **6** (R=Et) by an aldol-type condensation with benzaldehyde **7** in the presence of triethylamine and trimethylsilyl chloride (Scheme 2) [17]. This reaction proceeds completely diastereoselectively to yield only the *trans*-isomer. Analogously, binuclear complexes have been prepared from **6** and 1,3- and 1,4-phthaldialdehyde in good yields [17]. This type of condensation has



Scheme 2 Preparation of ethenylcarbene complexes **8** and **10** by aldol condensations [17–18]

also been used to access β-amino-substituted α,β-unsaturated Fischer carbene complexes like **10** [18].

The possibility of being involved in olefin metathesis is one of the most important properties of Fischer carbene complexes. [2+2] Cycloaddition between the electron-rich alkene **11** and the carbene complex **12** leads to the intermediate metallacyclobutane **13**, which undergoes [2+2] cycloreversion to give a new carbene complex **15** and a new alkene **14** [19]. The (methoxy)phenylcarbenetungsten complex is less reactive in this mode than the corresponding chromium and molybdenum analogs (Scheme 3).

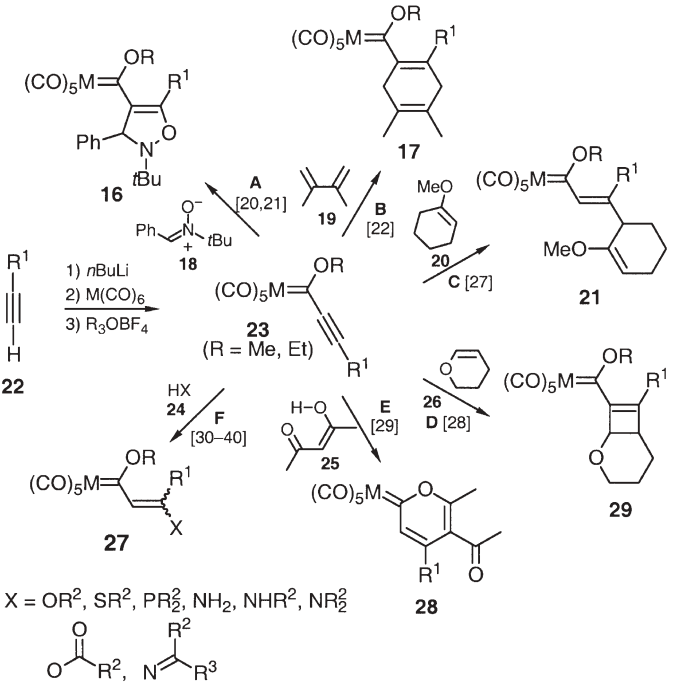


11/15	M	Solvent	Temp. [°C]	Time [h]	Yield **15** (%)
a	Cr	toluene	110	6	75
b	Mo	THF	66	4	57
c	W	THF	100	38	64

Scheme 3 Preparation of the ethenylcarbene complex **15** by olefin metathesis [19]

2.3 From Alkynylcarbene Complexes

In view of the strong electron-withdrawing influence of the pentacarbonylmetal moiety on the carbene ligand, it is obvious that in alkynyl-substituted complexes of type **23**, the triple bond is highly activated toward nucleophilic attack by a variety of reagents. Thus, 1,3-dipolar cycloadditions of nitrones such as **18** readily occur to yield the 2,3-dihydroisoxazolidinyl carbene complexes **16** highly chemo- and regioselectively (reaction mode A in Scheme 4) [20, 21]. Compared to a corresponding propargylic acid ester, the complexes **23** undergo this type of reaction faster. The triple bond reactivity of **23** is also drastically



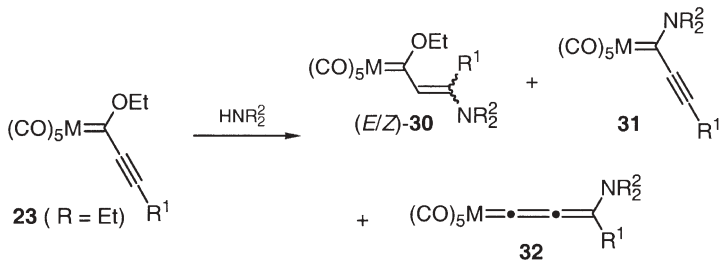
Scheme 4 Access to various α,β-unsaturated carbene complexes from alkynylcarbene complexes **23**. **A**: 1,3-Dipolar cycloaddition. **B**: Diels–Alder reaction. **C**: Ene reaction. **D**: [2+2] Cycloaddition. **E**: Michael-type addition followed by cyclization. **F**: Michael-type additions

enhanced for Diels–Alder reactions. Treatment of alkynyl Fischer carbene complexes **23** with a diene like **19** affords [4+2] cycloaddition products **17** in good to excellent yields (mode B) [22]. The investigations concerning the dienophilicity of 1-alkynylcarbene complexes of type **23** and regioselectivities in their Diels–Alder reactions with dienes extend well into the 1990s [23, 24]. Since 1-alkynylcarbene complexes **23** are significantly better dienophiles than the corresponding esters, they react at lower temperature, require shorter reaction times, and give better chemical yields [25, 26]. With enol ethers like **20** they undergo ene reactions to α,β-unsaturated complexes like **21** (mode C) [27] or [2+2] cycloadditions to cyclobutenyl complexes like **29** (mode D) [28]. These two modes can be competing with each other, depending on the substitution pattern on the enol ether and the substituents (R^1) on the complexes **23** [28].

In the presence of a catalytic amount of triethylamine, a readily enolizable carbonyl compound like acetylacetone (**25**) can undergo a Michael-type addition onto the triple bond of **23** with C–C bond formation, and subsequent 1,2-addition of the hydroxy group with elimination of an alcohol (MeOH or EtOH) to eventually yield a pyranylidene complex **28** (mode E) [29]. The most versatile access to β-donor-substituted ethenylcarbene complexes **27** is by Michael-type additions of nucleophiles, including alcohols [30–32], primary

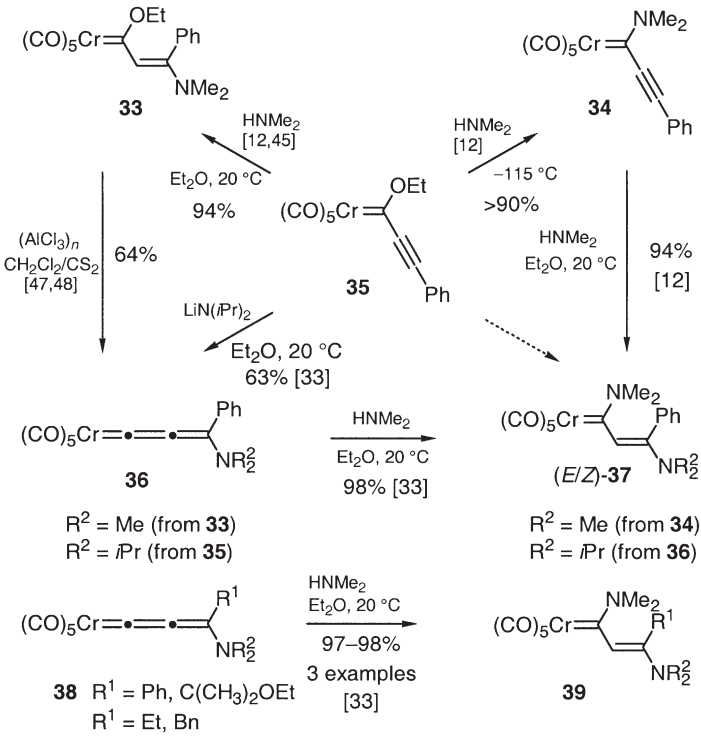
and secondary amines [30, 33–35], ammonia [30, 36], imines [37], phosphines [38, 39], thiols [30], and carboxylic acids [40] to alkynylcarbene complexes **23** (mode F). In some cases, like the addition of weaker nucleophiles such as alcohols and thiols, reaction rates and chemical yields can be improved by the presence of a catalytic amount of the corresponding sodium alkoxide or thiolate, respectively [30, 41].

This reaction mode of alkynylcarbene complexes of type **23** undoubtedly provides the most convenient access to β-amino-substituted α,β-unsaturated Fischer carbene complexes **27** (X=NH_2, NHR^2, NR^2_2). Fischer et al. reported the very first such addition of an amine to an alkynylcarbene complex of type **23** and observed a temperature-dependent competition between 1,4- and 1,2-addition [12]. In a later systematic study, de Meijere et al. found that in addition to the 1,4-addition products **30**, 1,2-addition–elimination (formal substitution) **31** and 1,4-addition–elimination products **32** can be formed (Scheme 5) [33]. The ratio of the three complexes **30**, **31**, and **32** largely depends on the polarity of the solvent, the reaction temperature, and the substituents on the alkyne (R^1) as well as the amine (R^2). If complexes **30** are desired, they can be obtained as single products or at least as the major products by careful choice of reaction conditions. Formation of the {[2-(dialkylamino)ethenyl]carbene}chromium complexes **30** is favored at low temperatures (–115 to 20°C) [41]. Room temperature is sufficient to give high yields of **30** from most complexes **23** and secondary amines. The complexes **30** are usually obtained as (*E*)-isomers with the exception of those with bulky substituents R^1 (e.g., R^1=*t*Bu [30] or R^1=$SiMe_3$ [42]). It is particularly favorable that these carbene complexes **30**, especially the ones with chromium, are easily accessible in a one-pot procedure from terminal alkynes **15**, hexacarbonylchromium, triethyloxonium tetrafluoroborate, and a secondary amine, generally in good to excellent yields [43, 44]. Formation of certain 1,2-addition–elimination products of type **31** is favored at low temperature [12, 45, 46]. (3-Dialkylaminoallenylidene)chromium complexes **32** were found as by-products, or even main products [30, 33], when bulky or highly basic secondary amines were added to the alkynylcarbene complexes **23** in polar solvents and at high temperature. With lithium amides, these metallacumulenes **32** could be produced as the sole products [33].



Scheme 5 Access to β-amino-substituted α,β-unsaturated Fischer carbene complexes **30** by Michael-type addition of amines to alkynylcarbene complexes **23** (R=Et) [30, 33]

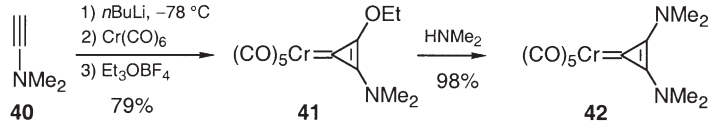
1,3-Diamino-substituted complexes of type **37** were first obtained by Fischer et al. [12] in two steps via the 1,2-addition–elimination product **34** from dimethylamine and **35** (Scheme 6). The (3-aminoallenylidene)chromium complexes **36**, which can be prepared either from **33** [47, 48] or directly from **35** [33], can also be transformed to 1,3-bis(dialkylamino)-substituted complexes of type **37** (e.g., R^2=*i*Pr) by treatment with dimethylamine in excellent yields [33]. Although the complex **37** is accessible by further reaction of the complex **34** with dimethylamine, and **34** itself stems from the reaction of **35** with dimethylamine, the direct transformation of **33** to **37** could not be achieved [12]. In spite of this, heterocyclic carbene complexes with two nitrogens were obtained by reactions of alkynylcarbene complexes **35** with hydrazine [49] and 1,3-diamines [50].



Scheme 6 Chemical relationships among the complexes **33**, **34**, **35**, **36**, and **37** [12, 33, 45, 47, 48]

In contrast to other terminal alkynes, the lithiated dimethylaminoethyne **40** does not give the corresponding alkynylcarbene but the cyclopropenylidene complex **41** (Scheme 7) [51]. Further addition of dimethylamine to **41** affords the substitution product **42** in excellent yield. This 2,3-bis(dimethylamino-cyclopropenylidene)pentacarbonylchromium (**42**) is extremely stable, and it cannot be transformed to the corresponding carbonyl compound, 2,3-bis

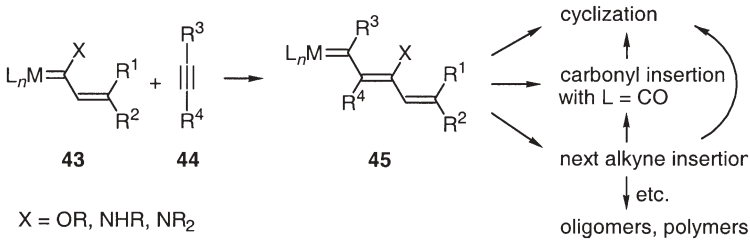
(dimethylamino)cyclopropenone, by oxidation with ceric ammonium nitrate (CAN) [52] or dimethyl sulfoxide (DMSO) [53].



Scheme 7 Synthesis of 2,3-bis(dimethylamino)cyclopropenylidene complex **42** [51]

3
Cocyclizations of α,β-Unsaturated Fischer Carbene Complexes with Alkynes

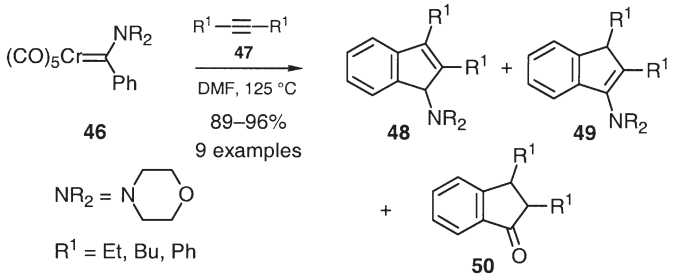
Most of the formal cycloaddition reactions of α,β-unsaturated Fischer carbene complexes **43** with alkynes **44** arise from a primary insertion product of type **45** (Scheme 8). The subsequent reactions of **45** depend mainly on the nature – electronic as well as steric – and pattern of substituents in **45**, brought in by the starting materials **43** and **44**. The first discovered reaction mode of **45** with an alkoxy group at the carbene center is that with carbonyl insertion and subsequent cyclization leading to alkoxycyclohexadienones or their enol tautomers, hydroquinone monoalkyl ethers, commonly known as the Dötz reaction or Dötz benzannelation reaction (see corresponding chapter in this book). Direct cyclization of **45** with subsequent reductive elimination, leading to five-membered rings may also occur, and five-membered ring products may also be formed with carbonyl insertion. In certain cases, **45** inserts another alkyne, and the resulting intermediate continues with carbonyl insertion or alkyne insertion before undergoing cyclization or oligomerization. All of these reaction modes may be classified as formal [k+m+n] cycloadditions, in which k, m, and n represent the respective number of atoms from the carbene ligand (k), the alkyne (m), and the carbonyl ligand (n). In the following subsections those cases with k>1, i.e., more than one atom from the carbene complexes participating in the cocyclizations, which do not lead to six-membered rings, will be described.



Scheme 8 Various modes of reaction of ethenylcarbene complexes **43** with alkynes **44** [11]

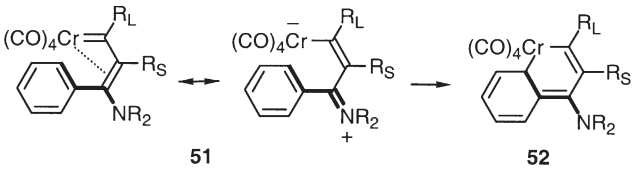
3.1
Formal [3+2] Cycloadditions

In 1986 Yamashida et al. found that the reaction of the (morpholino)phenylcarbene complex **46** with symmetric alkynes **47** gave the morpholinylindene derivatives **48** and **49**, as well as the indanones **50** derived from the latter by hydrolysis, in excellent yields (Scheme 9) [54]. This contrasts with the behavior of the corresponding (methoxy)phenylcarbene complex, which solely undergoes the Dötz reaction [55]. This transformation of the amino-substituted complex **46** apparently does not involve a CO insertion, which is an important feature of the Dötz benzannelation.



Scheme 9 Formation of indene derivatives from the complex **46** and alkynes **47** [54, 55]

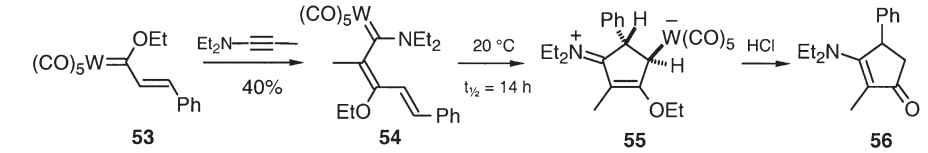
The non-CO-inserted products, the indenes **48/49**, almost certainly are formed by reductive elimination from chromadihydronaphthalenes **52**, which arise by 6π-electrocyclization from the alkyne-insertion intermediates **51** (Scheme 10). According to the study of Wulff et al. [56], an electron-donating dialkylamino group stabilizes a 1-chroma-1,3,5-triene **51**, and increases the electron density at the chromium atom. This in turn strengthens the Cr–CO bond and reduces the tendency of a *cis*-CO ligand to undergo insertion. The same selectivity for the formation of five-membered rings without CO insertion had also been observed by Dötz et al. [57].



Scheme 10 Suppression of the CO insertion by the electron-donating ability of a dialkyamino moiety [54–56]

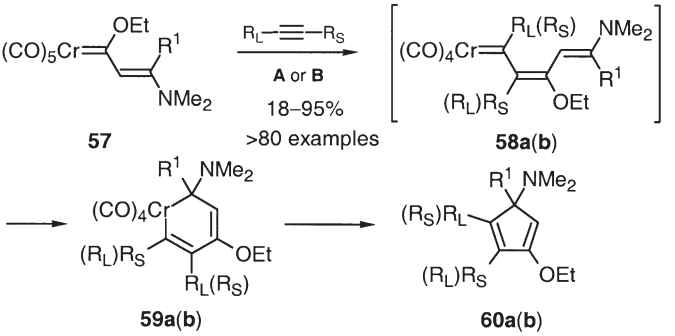
The formation of a formal [3+2] cycloaddition product **56** upon reaction of the ethoxystyryltungsten complex **53** with 1-diethylaminopropyne, as observed

by Aumann et al., shed some light on the mechanism (Scheme 11). The intermediate 2,4-bisdonor-substitued 1-tungsta-1,3,5-hexatriene **54**, formed by initial insertion of the alkyne into the carbene complex **53**, could be isolated in 40% yield [58]. It readily underwent 6π-electrocyclization at ambient temperature with a half-life of 14 h to give the zwitterionic cyclopentene derivative **55** which, upon treatment with hydrochloric acid, afforded the corresponding cyclopentenone **56** with loss of the pentacarbonyltungsten fragment [59].



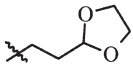
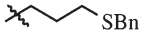
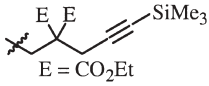
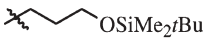
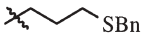
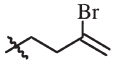
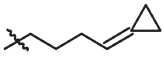
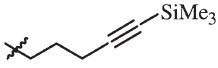
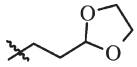
Scheme 11 Formation of the cyclopentenyl zwitterion derivative **55** from a 1-tungsta-2-diethylamino-1,3,5-hexatriene **54** [58, 59]

What later became a widely applicable, high yielding synthesis of 5-dialkylamino-3-ethoxy-1,3-cyclopentadienes of type **60** originally was observed only for the reaction of 3-cyclopropyl-substituted 3-dialkylamino-1-ethoxypropenylidenechromium complexes of type **57** (R^1=*c*Pr) with alkynes (Scheme 12) in THF [60] or in *n*-hexane [61]. This unique behavior was attributed to the well-known electron-donating property of the cyclopropyl group, which apparently disfavors the insertion of carbon monoxide at the stage of the alkyne insertion product **58**, and favors the 6π-electrocyclization to yield an intermediate chromacyclohexadiene **59**. The latter, just like the intermediate **52**, undergoes reductive elimination to yield the five-membered ring **60a**(**b**). As de Meijere et al. subsequently found out, this reaction mode becomes quite general with almost any kind of substituent – except for very bulky ones, which



Scheme 12 General synthesis of 5-dialkylamino-3-ethoxycyclopentadienes **60** from 3-dialkylamino-1-ethoxypropenylidenechromium complexes **57** and alkynes in a donor solvent. Conditions **A**: pyridine, 55–80 °C, 1.5–4 equiv. of the alkyne; **B**: MeCN, 80 °C, slow addition of 2–4 equiv. of the alkyne. For further details see Table 1 [43, 44, 60, 61]

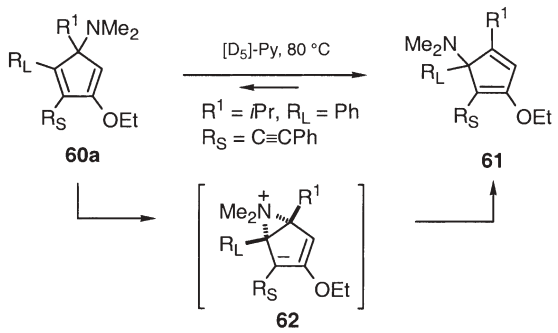
Table 1 Selected examples of 5-dialkylamino-3-ethoxycyclopentadienes **60a**(**b**) obtained from 3-dialkylamino-1-ethoxypropenylidenechromium complexes **57** and alkynes in a donor solvent. For details see Scheme 12 [43, 44, 60, 61]

Entry	R^1	Condition	R_L	R_S	Yield (%) **60a/60b**
1	Me	**A**	Me	Me	82/0
2	Me	**A**		H	86/0
3	*n*Pr	**A**	Me	Me	95/0
4	*n*Pr	**A**	Ph	Ph	80/0
5	*n*Pr	**A**		H	75/11
6	*n*Pr	**B**		H	81/0
7	*n*Pr	**A**	Me	Me	77/0
8	*c*Pr	**A**	Me	Me	84/0
9		**A**	Me	Me	91/0
10		**A**	Me	H	78/0
11		**A**	Me	Me	79/0
12		**A**	Me	Me	69/0
13		**A**	$SiMe_3$	H	48/6
14		**A**	Me	H	88/0

lead to different types of products (see below) – when the reaction of **57** with an alkyne is carried out in a donor-type solvent such as pyridine or acetonitrile (Scheme 12 and Table 1) [43, 44]. The regioselectivity largely depends on the relative steric bulk of the substituents R^1 in the complexes **57** and R_L, R_S in the alkynes, and in the former they have more influence than in the latter [44]. Other factors, including concentrations of the complexes **57** and applied alkynes, and the electronic properties of substituents on the alkynes, do not play important roles [62].

Cocyclizations of internal alkynes and carbene complexes **57** with larger substituents R^1 (e.g., R^1=*i*Pr) not only lead to formation of an increased proportion of the regioisomers **60b**, but also to that of the isomeric cyclopentadienes **61**, which would result from **60a** by 1,2-migration of the dimethylamino

group via the bridged zwitterionic intermediate **62** (Scheme 13) [44]. The fact that isomeric cyclopentadienes **61** are formed only when the less sterically demanding substituent R_S in the incoming alkyne has an electron-withdrawing effect is in line with this assumption, and not with a 1,5-migration of the dimethylamino functionality.

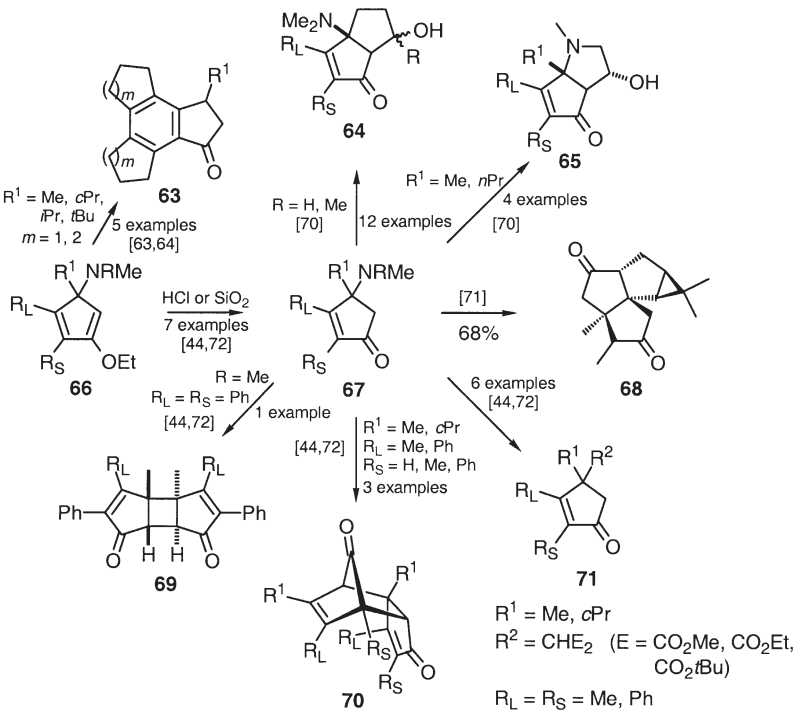


Scheme 13 Possible mode of formation of the cyclopentadiene **61** isomeric with **60a** by 1,2-migration of the dimethylamino group via a bridged zwitterionic intermediate **62** [44]

Variously substituted 5-amino-3-ethoxycyclopentadienes **66** have been applied toward the preparation of more complex structures to demonstrate their versatility in organic synthesis. When dienyl-substituted cyclopentadienes of type **66** (R_L, R_S=cycloalkene) are generated from the reaction of correspondingly substituted complexes of type **57** with conjugated 1,5-dien-3-ynes, the trisannelated benzene derivatives **63** were obtained by a sequence of 6π-electrocyclization, twofold 1,*n*-hydrogen shifts, elimination of a dimethylamine, 1,5-hydrogen shift, and finally hydrolysis (Scheme 14) [63, 64]. Compared to the traditional approaches to trisannelated benzene derivatives of type **63** by aldol condensation [65–69], this method has the advantages of milder conditions and the provision of additional functionality. It remains to be tested whether skeletons with two annelated small rings would be accessible by this new method. Because of their enol ether moieties, the cyclopentadienes **66** can be easily hydrolyzed to the corresponding cyclopentenones **67** in excellent yields by treatment with a catalytic amount of hydrochloric acid [44]. With this in mind, de Meijere et al. developed very short and direct accesses to bicyclo[3.3.0]oct-2-en-4-ones **64** and 8-azabicyclo[3.3.0]octenones **65** by intramolecular aldol reactions of dicarbonyl compounds derived from cyclopentenones **67** with an acetal-protected aldehyde or ketone carbonyl group in the substituent R^1 or R, respectively [70]. This type of transformation has been applied toward short syntheses of angular triquinanes like **68** in an enantiomerically pure form [71], as well as other complex oligocycles [63, 64].

The dialkylamino, especially the dimethylamino, group in a cyclopentenone of type **67** can be alkylated with methyl iodide to yield a quaternary ammonium salt. Upon treatment with a base, these quaternary ammonium salts undergo

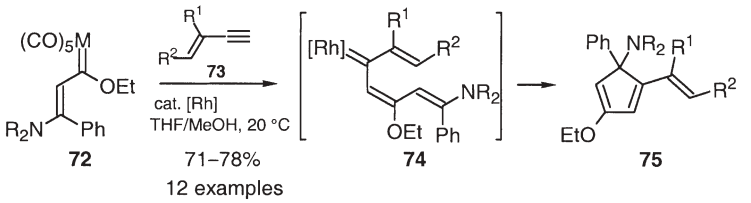
Hofmann elimination to correspondingly substituted cyclopentadienones which, depending on the nature and the nucleophilicity of the base as well as the nature of the substituents R_L and R_S, undergo [2+2] or [4+2] cyclodimerization or in situ Michael addition to yield compounds **69**, **70**, and **71**, respectively (Scheme 14) [44, 70].



Scheme 14 Some applications of 5-amino-3-ethoxycyclopentadienes **66** to the syntheses of cyclopentanoid skeletons [44, 63, 64, 70–72]

Recently, Aumann et al. reported that rhodium catalysts enhance the reactivity of 3-dialkylamino-substituted Fischer carbene complexes **72** to undergo insertion with enynes **73** and subsequent formation of 4-alkenyl-substituted 5-dialkylamino-2-ethoxycyclopentadienes **75** via the transmetallated carbene intermediate **74** (Scheme 15, Table 2) [73]. It is not obvious whether this transformation is also applicable to complexes of type **72** with substituents other than phenyl in the 3-position. One alkyne **73**, with a methoxymethyl group instead of the alkenyl or phenyl, i.e., propargyl methyl ether, was also successfully applied [73].

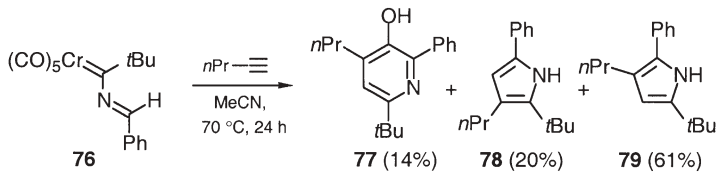
Alkylideneaminocarbene complexes **76**, which are aza analogs of alkenylcarbene complexes, upon reaction with alkynes primarily give formal [3+2] cycloadducts analogous to the 1-aminocarbene complexes (Scheme 16) [74, 75]. Aumann et al. proposed that this should be considered as a formal 1,3-dipo-



Scheme 15 Formation of 4-alkenyl(phenyl)-substituted 5-dialkylamino-2-ethoxycyclopentadienes **75** via transmetallated alkyne-inserted rhodium-carbene complexes **74** [73]. For further details see Table 2

Table 2 Formation of cyclopentadienyl derivatives **75** via transmetallated alkyne-inserted rhodium-carbene complexes (see Scheme 15)

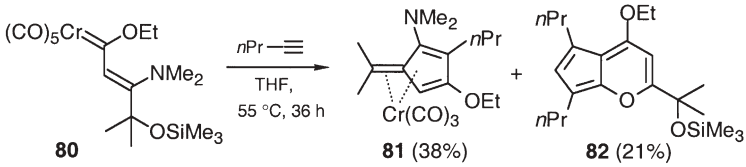
Entry	M	NR_2	R^1	R^2	$[(COD)RhCl]_2$ Yield (%)	$[(CO)_2RhCl]_2$ Yield (%)	$RhCl_3 \cdot 3H_2O$ Yield (%)
1	Cr	NMe_2	Me	H			76
2	W	NMe_2	Me	H	53	74	78
3	W	NEt_2	Me	H			74
4	Cr	Morpholine	Me	H			74
5	W	Morpholine	Me	H	58	75	76
6	Cr	NMe_2	$-(CH_2)_4-$				72
7	W	NMe_2	$-(CH_2)_4-$				73
8	W	NEt_2	$-(CH_2)_4-$		61		71
9	W	Morpholine	$-(CH_2)_4-$		60		71
10	W	(+)-Ephedrine	Me	H			78
11	W	(+)-Prolinole	Me	H			75
12	W	NHMe	Me	H		0	0
13	W	NHEt	Me	H		0	0
14	W	NMe_2	$-(CH)_4-$				76
15	W	NEt_2	$-(CH)_4-$				77



Scheme 16 Formation of pyrroles **78** and **79** from the benzylideneaminocarbene complex **76** and 1-pentyne [74, 75]

lar cycloaddition. The product distribution from the reaction of **76** with 1-pentyne to a certain extent depends on the solvent used [74]. When hexane is applied instead of acetonitrile, the ratio of the formal [3+2+1] **77** to formal [3+2] cycloadducts **78** and **79** does not significantly change, but the ratio of the regioisomers **78** and **79** does.

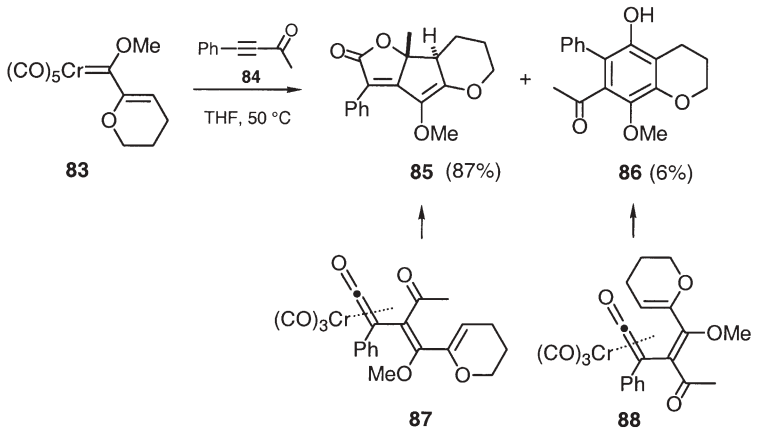
The formation of the tricarbonylchromium-complexed fulvene **81** from the 3-dimethylamino-3-(2′-trimethylsilyloxy-2′-propyl)propenylidene complex **80** and 1-pentyne also constitutes a formal [3+2] cycloaddition, although the mechanism is still obscure (Scheme 17) [76]. The η^6-complex **81** must arise after an initial alkyne insertion, followed by cyclization, 1,2-shift of the dimethylamino group, and subsequent elimination of the trimethylsilyloxy moiety. Particularly conspicuous here are the alkyne insertion with opposite regioselectivity as compared to that in the Dötz reaction, and the migration of the dimethylamino functionality, which must occur by an intra- or intermolecular process. The mode of formation of the cyclopenta[*b*]pyran by-product **82** will be discussed in the next section.



Scheme 17 Formation of the (tricarbonylchromium)-complexed fulvene **81** and the cyclopenta[*b*]pyran **82** from the 3-dimethylamino-3-(2′-trimethylsilyloxy-2′-propyl)propenylidene complex **80** and 1-pentyne [76]

3.2
[3+4+1] and [3+2+2+1] Cocyclizations

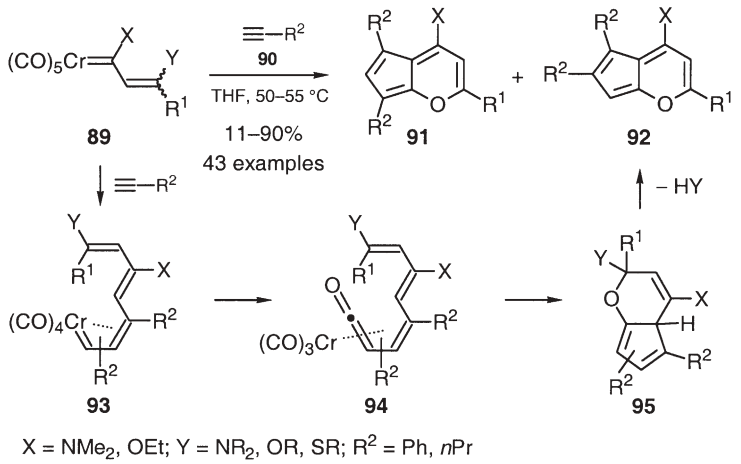
Reaction of the dihydropyranyl-substituted complex **83** with a conjugated internal alkynone **84** affords the Dötz-type formal [3+2+1] cycloadduct **86** in only 6% yield. The major product is the tricycle **85** as the result of a formal [3+4+1] cycloaddition with incorporation of the ynone carbonyl group (Scheme 18) [77].



Scheme 18 Formation of tricyclic product **85** via a von Halban–White-type cyclization [77]

This crisscross or von Halban–White-type cyclization product is formed from the (*E*)-configured intermediate **87**, which cannot undergo the 6π-electrocyclization like the (*Z*)-configured isomer **88**, to yield the benzannelation product **86** [78, 79]. While the diastereoselectivity of the alkyne insertion must have been controlled by the electronic and not the steric factors of the substituents on the alkyne, the *anti*-configuration of the tricyclic system **85** was confirmed by an X-ray structure analysis [77].

Steric effects must play a major role in determining the configurations of 2-donor-substituted ethenylcarbenechromium complexes **89** obtained by Michael-type additions onto alkynylcarbene complexes, and of their alkyne-insertion products. With bulky substituents in the 2′-position, complexes **89** are mostly (*Z*)-configured and yield (*Z*,*E*)-configured 1-chroma-1,3,5-hexatrienes which cannot easily undergo 6π-electrocyclization. They rather insert another molecule of the alkyne **90** and carbon monoxide to give **93** and **94**, respectively, which undergo intramolecular [4+2] cycloaddition and subsequent elimination of HY to the regioisomeric cyclopenta[*b*]pyrans **91** and **92** in yields up to 90% (Scheme 19, Table 3) [80]. In most cases, the isomers **91** are formed as major or even single products. However, the second alkyne insertion into complexes **89** can occur with incomplete regioselectivity, thus the two isomeric products can be formed. High chemical yields in this kind of transformation are obtained from complexes **89** with a tertiary or a bulky secondary substituent (R^1), a weak donor substituent X (e.g., OEt is better than NMe_2), and a good donor group Y (e.g., NR_2>OR≥SR) [41]. This new synthesis of cyclopenta[*b*]pyrans from easily prepared starting materials is superior to previously developed accesses to these so-called pseudoazulenes, which show unusual photophysical properties. Besides strong absorptions in the UV region, they also exhibit a broad absorption band in the visible light region with extinction coefficients ε of about 1,000.



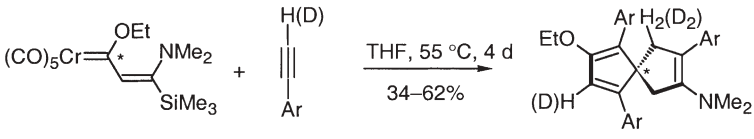
Scheme 19 Formation of cyclopenta[*b*]pyrans **91** and **92** by a [3+2+2+1] cocyclization [41, 80]. For further details see Table 3

Table 3 Selected examples of cyclopenta[*b*]pyrans **91** and **92** formed by [3+2+2+1] cocyclizations (see Scheme 19)

Entry	R^1	X	Y	R^2	Product	Yield (%)
1	Ph	OEt	NMe_2	Ph	**91a**	24
2	Ph	OEt	NBn_2	Ph	**91a**	48
3	Ph	OEt		Ph	**91a**	43
4	Ph	OEt	$N(i\text{Pr})_2$	Ph	**91a**	17
5	Ph	OEt	NMe_2	*n*Pr	**91b**	19
6	Ph	OEt	$N(i\text{Pr})_2$	*n*Pr	**91b**	11
7	$C(CH_3)_2OEt$	NMe_2	NBn_2	Ph	**91c**	39
8	$C(CH_3)_2OEt$	OEt	NMe_2	Ph	**91d**	51
9	$C(CH_3)_2OEt$	OEt	NBn_2	Ph	**91d**	68
10	$C(CH_3)_2OEt$	OEt	OEt	Ph	**91d**	27
11	$C(CH_3)_2OEt$	OEt	OPh	Ph	**91d**	28
12	$C(CH_3)_2OEt$	OEt	OBn	Ph	**91d**	18
13	$C(CH_3)_2OSiMe_3$	NMe_2	NBn_2	Ph	**91e**	28
14	$C(CH_3)_2OSiMe_3$	OEt	NMe_2	Ph	**91f**	90
15	$C(CH_3)_2OSiMe_3$	OEt	NBn_2	Ph	**91f**	78
16	$CHCH_3OSi\text{t}BuPh_2$	OEt	NMe_2	Ph	**91g/92g**	39/2
17	$CHCH_3OSi\text{t}BuPh_2$	OEt	NBn_2	Ph	**91g/92g**	74/22
18		OEt	NMe_2	*n*Pr	**91h**	33
19		OEt	NMe_2	Ph	**91i**	84
20		OEt	NBn_2	Ph	**91j/92j**	44/37
21	adamantyl	OEt	NMe_2	Ph	**91k**	56
22	adamantyl	OEt	NBn_2	Ph	**91k**	47

3.3 [3+2+2+2] Cocyclizations

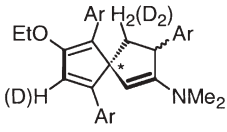
The novel highly substituted spiro[4.4]nonatrienes **98** and **99** are produced by a [3+2+2+2] cocyclization with participation of three alkyne molecules and the (2′-dimethylamino-2′-trimethylsilyl)ethenylcarbene complex **96** (Scheme 20). This transformation is the first one ever observed involving threefold insertion of an alkyne and was first reported in 1999 by de Meijere et al. [81]. The structure of the product was eventually determined by X-ray crystal structure analysis of the quaternary ammonium iodide prepared from the regioisomer **98** (Ar=Ph) with methyl iodide. Interestingly, these formal [3+2+2+2] cycloaddition products are formed only from terminal arylacetylenes. In a control experiment with the complex **96** ^{13}C-labeled at the carbene carbon, the ^{13}C label was found only at the spiro carbon atom of the products **98** and **99** [42].



96 **97** **98**

Ar	Yield **98**+**99** (%)	Ratio **98**:**99**
C_6H_5	62	1.8:1
4-PhC_6H_4	34	4.5:1
4-$MeOC_6H_4$	37	2.5:1
3,5-$(Me)_2C_6H_3$	48	1.6:1

+



99

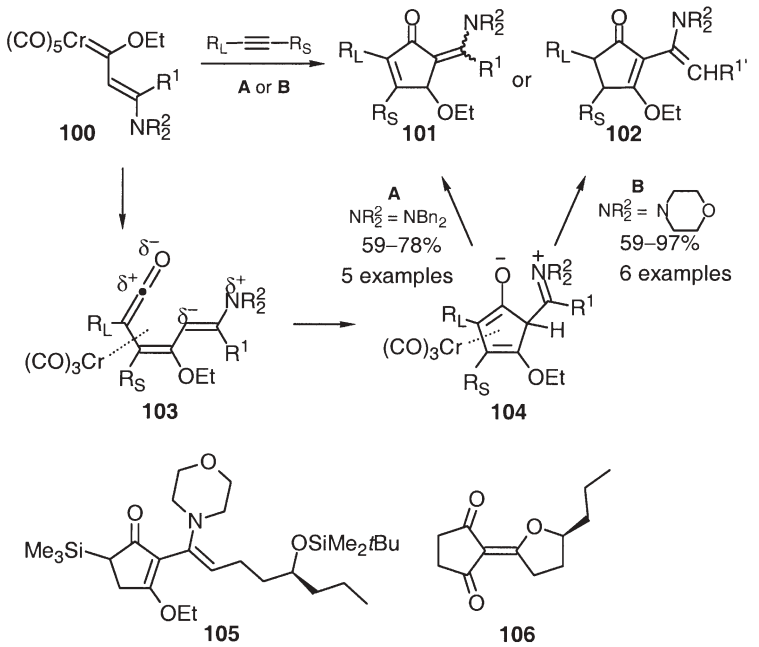
Scheme 20 Formation of highly substituted spiro[4.4]nonatrienes **98** and **99** from the (2′-dimethylamino-2′-trimethylsilyl)ethenylcarbene complex **96** and arylacetylenes **97** [42, 81]

Terminally deuterium-labeled phenylacetylene was also used to elucidate the possible mechanism of this reaction. In view of all these results, a rationalization for the loss of the trimethylsilyl and the migration of the ethoxy group from its original position in the complex **96** has been put forward. Due to the contribution of the conjugated diarylcyclopentadiene moiety in **98** and **99**, these molecules showed intense fluorescence with a relatively high quantum yield of 46%.

3.4 [2+2+1] Cocyclizations

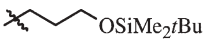
Strikingly, (2′-dialkylamino)ethenylcarbene complexes **100** (type **57**, but with a morpholinyl or dibenzylamino group) can also undergo a [2+2+1] cocyclization with insertion of carbon monoxide like in the classical Dötz reaction, yet with only two carbons of complexes **100** participating in the formation of the ring, thus yielding a methylenecyclopentenone **101** or **102**. After insertion of an alkyne and a CO molecule, the resulting dienylketene complex **103**, due to its 1,5-dipolar properties, undergoes a 1,5-cyclization rather than a 6π-electrocyclization to form the five-membered ring **104** (Scheme 21) [82, 83]. Depending on the reaction conditions and the nature of the amino substituent, either the aminomethylenecyclopentenone **101** or the 2-(aminoalkenyl)cyclopentenone **102** is formed by a hydrogen shift and loss of the tricarbonylchromium fragment. The products **101** are obtained as mixtures of (*E*)- and (*Z*)-isomers, with their ratios depending on the nature of the substituents. In all cases, the (*Z*)-isomers of **101** were obtained as the major products. Starting from the enantiomerically pure (*S*)-5-(*tert*-butyldimethylsilyl)-1-octyne, the cyclopentenone **105**, which is of type **102**, was prepared along such a route and applied to a short synthesis of the natural product (–)-oudenone **106** with 92% *ee* [83] (Table 4).

Under the same conditions, but in moist solvents, complexes of type **100** with terminal alkynes **90** gave 2-acyl-3-amino- **107** and 2-acyl-3-ethoxycy-

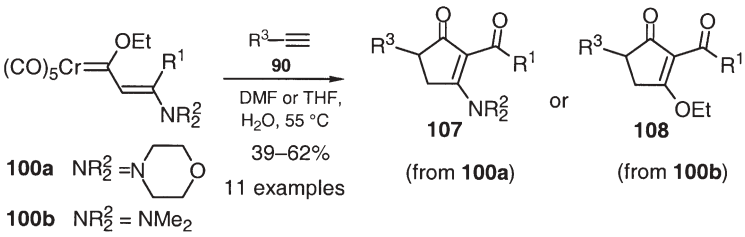


Scheme 21 Formation of 5-(aminomethylene)cyclopentenones **101** and 2-(1′-aminoalkenyl)-cyclopentenones **102** by formal [2+2+1] cycloadditions. Conditions **A**: THF, 50–55 °C. **B**: THF/MeCN (9/1), 65 °C [82, 83]. For further details see Table 4

Table 4 Selected examples of cyclopentenones **101** and **102** formed from complexes **100** (see Scheme 21)

Entry	R^1	Condition	R_L	R_S	Product	Yield (%)
1	*n*Pr	**A**	Ph	Ph	**101a**	68
2	*n*Pr	**A**	Me	Me	**101b**	78
3	*n*Pr	**A**	$-(CH_2)_6-$		**101c**	75
4	*c*Pr	**A**	Ph	Ph	**101d**	59
5	*c*Pr	**A**	$-(CH_2)_6-$		**101e**	62
6	*n*Pr	**B**	*n*Pr	H	**102a**	82
7	*n*Pr	**B**	Ph	H	**102b**	97
8	Me	**B**	$SiMe_2tBu$	H	**102c**	72
9		**B**	$SiMe_2tBu$	H	**102d**	69

clopentenones **108** (Scheme 22). The latter are also formed via the intermediates **104** (NR_2^2=NMe_2; R_S=H) and subsequent hydrolysis [84]. Formation of **107** (NR_2^2=morpholine), however, not only requires hydrolysis, but also a formal shift of the morpholine group which probably occurs by 1,4-addition of morpholine to **108** with subsequent 1,4-elimination of ethanol [85].



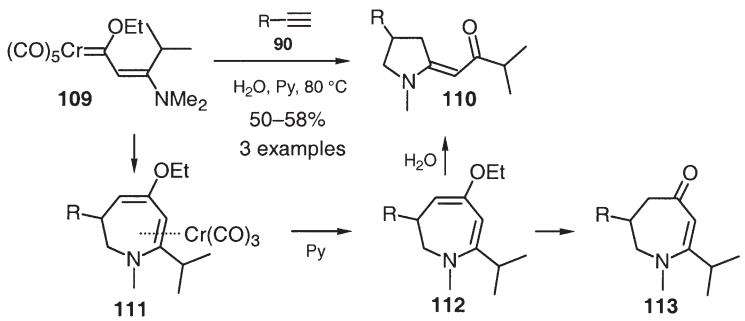
Scheme 22 Formation of 2-acyl-3-amino- **107** and 2-acyl-3-ethoxycyclopentenones **108** in moist solvents [84, 85]. For further details see Table 5

Table 5 Selected examples of cyclopentenone derivatives **107** and **108** formed from complexes **100a**,**b** in moist solvents (see Scheme 22)

Entry	R^1	NR^2_2	R^3	Product	Yield (%)
1	*n*Pr	Morpholine	*n*Pr	**107a**	68
2	*n*Pr	Morpholine	*t*Bu	**107b**	78
3	*n*Pr	Morpholine	$SiMe_2t$Bu	**107c**	75
4	Ph	Morpholine	*n*Pr	**107d**	59
5	Ph	Morpholine	*t*Bu	**107e**	62
6	Ph	Morpholine	$SiMe_2t$Bu	**107f**	82
7	*i*Pr	NMe_2	*t*Bu	**107g**/**108g**	15/47

3.5 [5+2] Cocyclizations

The reactions of the isopropyl-substituted 3-dimethylaminopropenylidenechromium complex **109** with terminal alkynes **90** bearing a bulky substituent (e.g., R=*tert*-butyl, mesityl, adamantyl etc.), in the presence of moist pyridine, yield 2-(acylmethylene)pyrrolidines **110** (Scheme 23) [84]. The dihydroazepinetricarbonylchromium complexes **111** were found to be the key

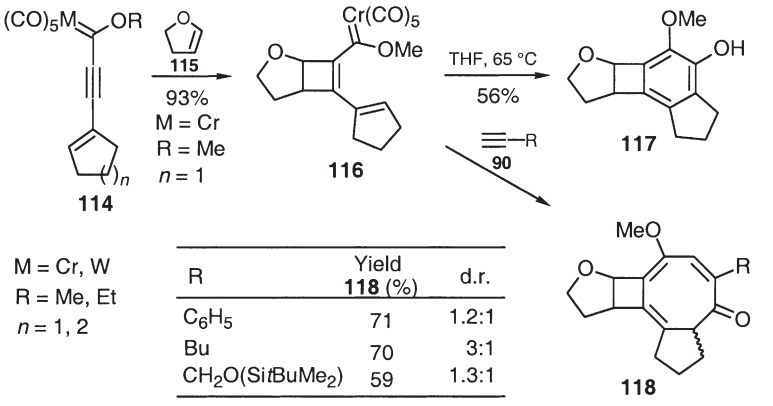


Scheme 23 Formation of tetrahydroazepinones **113** and methylenepyrrolidines **111** by a formal [5+2] cycloaddition with C–H activation [85]

intermediates in this transformation. The complexes **111** could be synthesized from the same starting materials in the presence of 1 equiv. of triphenylphosphine in THF. The formation of these unusual complexes **111** was proposed to occur with initial insertion of the alkyne into the complex **109**, activation by the chromium fragment of a carbon–hydrogen bond in the dimethylamino functionality, and insertion into it, thus leading to ring closure to give **111** [84]. The structure of **111** was rigorously proved by X-ray crystal structure analysis of a derivative with R=mesityl. It shows that the tricarbonylchromium fragment is η^5-coordinated with the aminodienyl unit of the dihydroazepine. Treatment of the complex **111** with anhydrous pyridine afforded decomplexed dihydroazepines **112** which were isolated as the corresponding ketones **113**. However, in the presence of moist pyridine, **111** underwent hydrolysis with ring contraction to yield methylenepyrrolidines **110**.

3.6
[5+2+1] Cocyclizations

Barluenga et al. reported interesting transformations of the 2-oxabicyclo-[3.2.0]heptenyl-substituted complex **116**, which was prepared by a [2+2] cycloaddition of the ethynylcarbene complex **114** to dihydrofuran **115** (Scheme 24). Upon heating the tricyclic complex **116** at 65 °C, CO insertion with subsequent 6π-electrocyclization in the sense of an intramolecular Dötz reaction occurs, to yield the tetracyclic catechol monoether **117** [86]. This result is quite surprising since 1-metalla-1,3,5-hexatrienes usually undergo 6π-electrocyclization without CO insertion (cf. Scheme 32). On the other hand, the complex **116** upon intermolecular reaction with a terminal alkyne, CO insertion, and subsequent cyclization of an intermediate trienylketenyl derivative gave bisannelated methoxycyclooctatrienones **118** [87]. This overall transformation constitutes a formal [5+2+1] cycloaddition or – in other terms – a vinylogous Dötz reaction.

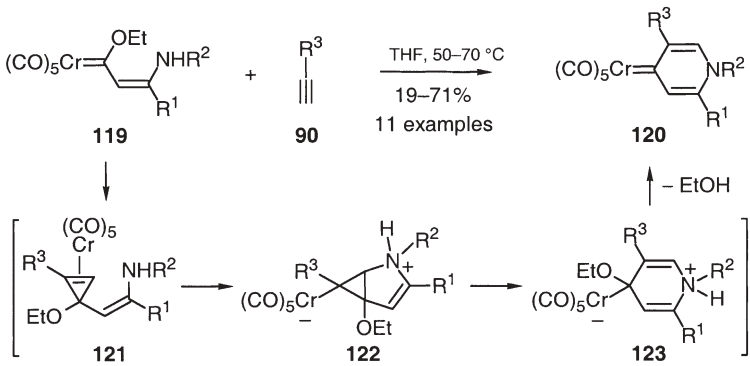


R	Yield **118** (%)	d.r.
C_6H_5	71	1.2:1
Bu	70	3:1
$CH_2O(SitBuMe_2)$	59	1.3:1

Scheme 24 Formation of a bisannelated methoxycyclooctatrienone **118** by a formal [5+2+1] cycloaddition [86, 87]

3.7
[4+2] Cocyclizations

Upon heating an alkenylidenechromium complex **119** substituted with a secondary 3-amino group, in the presence of a terminal alkyne **90** in THF, 4-(1*H*)-pyridinylidene complexes of type **120** were formed with a high degree of regioselectivity (Scheme 25) [76, 88]. This reaction mode is completely different from that of an alkenylidenechromium complex with a tertiary amino substituent in the 3-position. The formation of **120** can be rationalized by way of a 4π-electrocyclization to yield a 3-aminoalkenyl-3-ethoxycyclopropenylpentacarbonylchromium complex **121**. The alkenylcyclopropene derivative **121** would be expected to undergo a regioselective intramolecular addition of the amino group onto the cyclopropene double bond, with attack at the least substituted carbon atom to give a bicyclic zwitterionic intermediate **122**. Ring expansion with opening of the three-membered ring and migration of the carbonylchromium residue would lead to **123**, from which 1,4-elimination of ethanol would provide the pyridinylidene complex **120**. The pentacarbonylchromium fragment can be removed from these by treatment with HBF_4 to afford the corresponding pyridinium salts [88].



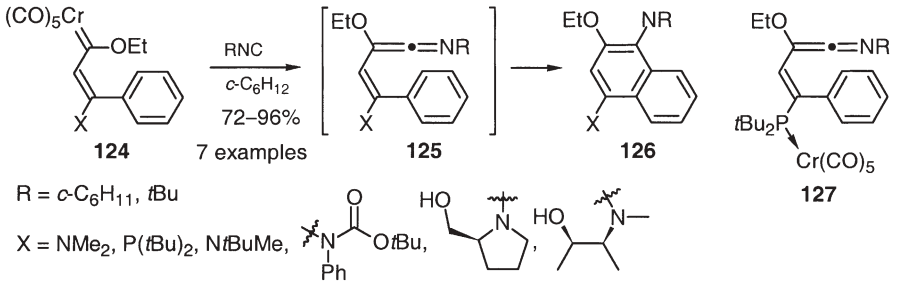
R^1 = *n*Bu, Ph, $CMe_2(OSiMe_3)$; R^2 = Me, *i*Pr, Ph, Bn; R^3 = *n*Bu, Ph

Scheme 25 Formation of 4-(1*H*)-pyridinylidene complexes **120** by a formal [4+2] cycloaddition [76, 88]

3.8
Cocyclizations with Aza- and Phosphaalkynes

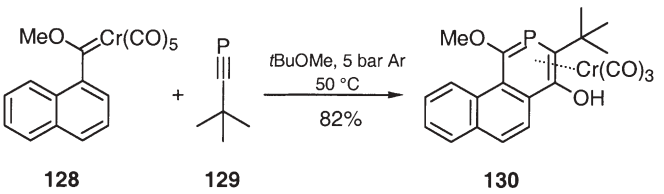
Aumann et al. showed that 1,2,4-tridonor-substituted naphthalenes, such as **126**, are accessible from 3-donor-substituted propenylidenecarbene complexes **124** containing a (*Z*)-positioned 3-phenyl substituent and isocyanide (Scheme 26). These transformations constitute formal [5+1] cycloadditions [39, 89, 90]. Since isocyanides are strongly coordinating ligands on chromium, at least

2 equiv. has to be applied for this reaction, which in most cases proceeds under mild conditions, even at 20 °C, and affords good to excellent yields (72–96%). The proposed key intermediates, the ketenimine complexes **125** (with coordination of $(CO)_4Cr(RNC)$ at the imine moiety), cannot be isolated, but rapidly undergo 6π-electrocyclization and subsequent tautomerization to form naphthalenes **126.** (*Z*)-Configured ketenimines **125** with an acylamino substituent in the 4-position and the complex **127**, however, can be isolated in excellent yields from the reaction of the corresponding complexes **124** with *tert*-butyl isocyanide. Upon heating, these phenylethenylketimines of type **125** and complex **127**, still (*Z*)-configured, also gave naphthalenes **126** in excellent yields.



Scheme 26 Cocyclizations of 3-phenyl-substituted propenylidenechromium complexes **124** with isocyanides [39, 89, 90]

Kinetically stabilized phosphaalkynes have also been applied as reaction partners for α,β-unsaturated Fischer carbene complexes. Thus, reaction of the (1-naphthyl)carbenechromium complex **128** with 3,3-dimethyl-1-phosphabutyne (**129**) afforded the substituted 3-phosphaphenanthrenetricarbonylchromium complex **130** in very good yield (Scheme 27) [91]. A kinetic investigation disclosed that **129** reacts six times faster than its carbon analog, 3,3-dimethylbutyne, in this same transformation. According to an X-ray crystal structure analysis, one carbonyl group of the $Cr(CO)_3$ unit in **130** is nearly eclipsed with the phosphorus atom, apparently in order to minimize steric interactions between the ring substituents and the carbonyl ligands. The coordination of the phosphinine ring to the tricarbonylchromium moiety is very strong. The

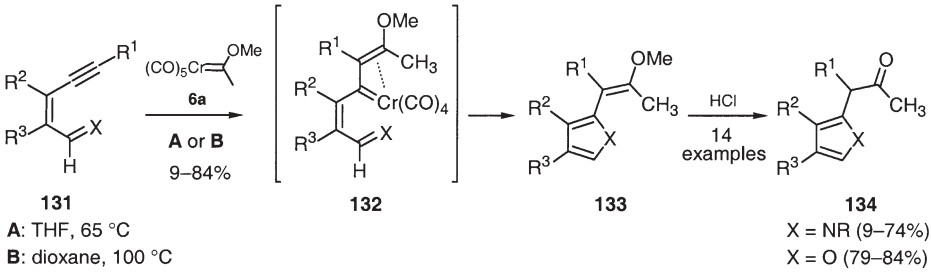


Scheme 27 Cocyclization of the 1-naphthylcarbene complex **128** with *tert*-butylphosphaalkyne **129** [91]

complex has to be heated in refluxing toluene to give the decomplexed 3-phosphaphenanthrene, which can also be obtained in significantly better yield (95%) by treatment of the complex **130** with CO under pressure (30 bar) at 70 °C.

3.9 Cocyclizations of In Situ Generated Alkenylcarbene Complexes

The insertion of alkynes into a chromium–carbon double bond is not restricted to Fischer alkenylcarbene complexes. Numerous transformations of this kind have been performed with simple alkylcarbene complexes, from which unstable α,β-unsaturated carbene complexes were formed in situ, and in turn underwent further reactions in several different ways. For example, reaction of the 1-methoxyethylidene complex **6a** with the conjugated enyne-ketimines and -ketones **131** afforded pyrrole [92] and furan **134** derivatives [93], respectively. The alkyne-inserted intermediate **132** apparently undergoes 6π-electrocyclization and reductive elimination to afford enol ether **133**, which yields the cycloaddition product **134** via a subsequent hydrolysis (Scheme 28). This transformation also demonstrates that Fischer carbene complexes are highly selective in their reactivity toward alkynes in the presence of other multiple bonds (Table 6).

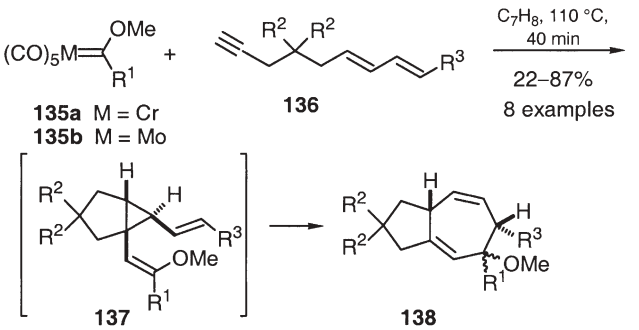


Scheme 28 Synthesis of pyrrole and furan derivatives **134** from the 1-methoxyethylidenechromium complex **6a** and enyneketimines or -ketones **131** [92, 93]. For further details see Table 6

Table 6 Synthesis of pyrrole and furan derivatives **134** (see Scheme 28)

Entry	Conditions	R^1	R^2	R^3	X	Product	Yield (%)
1	**B**	*n*Bu	$-(CH_2)_3-$		O	**134a**	84
2	**B**	H	$-(CH_2)_3-$		O	**134b**	79
3	**A**	*n*Bu	Ph	H	$NNMe_2$	**134c**	62
4	**A**	*n*Bu	Ph	H	NTs	**134d**	37
5	**A**	*n*Bu	Ph	H	NMs	**134e**	35
6	**A**	*n*Bu	Ph	H	NBn	**134f**	9
7	**A**	*n*Bu	H	Et	$NNMe_2$	**134g**	74

Combinations of alkyne insertion and subsequent intramolecular [2+1] cycloaddition to produce 1-(2-oxopropyl)-3-oxabicyclo[3.1.0]hexanes and their azaanalogs from 1-methoxyethylidenecarbenechromium complex **6a** and nonconjugated enynes have been reported [94, 95]. In view of this reaction mode, Harvey et al. used 1,3-dien-8-ynes **136** instead of nonconjugated enynes to generate 1,6-dialkenylbicyclo[3.1.0]hexanes **137**, which immediately underwent Cope rearrangement to furnish hexahydroazulenes **138** (Scheme 29) [96]. The 1-methoxyalkylidenemolybdenum complexes **135b** gave better yields (up to 87%) than their chromium analogs **135a**. The diastereomers of **138** with the methoxy and the R^3 substituents on the same side of the seven-membered ring were obtained as major products.

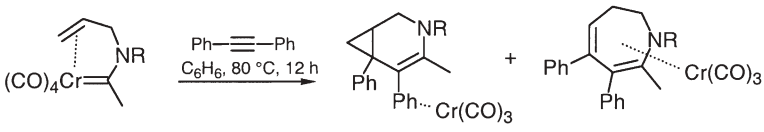


M	R^1	R^2	R^3	(%)	(*E*/*Z*)
Mo	*n*Bu	H	CO_2Et	87	1 : 4.8
Mo	*n*Bu	CO_2Me	CO_2Me	81	1 : 4.8
Cr	Me	H	CO_2Et	24	1 : 2.1
Cr	*n*Bu	H	CO_2Et	22	1 : 2.1

Scheme 29 Synthesis of substituted hexahydroazulenes **138** from simple 1-methoxyalkylidene complexes **135** and 1,3-dien-8-ynes **136** [96]

The η^2-(allylamino)methylcarbenetetracarbonylchromium complex **139** is formed upon heating of the corresponding pentacarbonyl complex in THF (Scheme 30). The 1-allylaminocarbene complex **139** also undergoes insertion of diphenylacetylene and subsequent intramolecular cyclopropanation to form the 2-(tricarbonylchromiumphenyl)-substituted azabicyclo[4.1.0]heptenes **140** as well as their ring-enlargement products **141**. The $Cr(CO)_3$ unit sits on the more electron-rich phenyl moiety in **140**. The amount of ring-enlargement product **141** varies with the nature of the substituent R on the nitrogen, with benzyl apparently facilitating this ring enlargement [97–99].

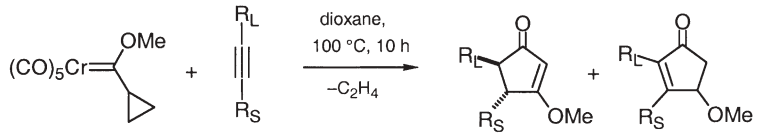
The simple cyclopropylmethoxycarbenechromium complex **142** reacts with alkynes to afford cyclopentenones **143** and **144** via the cyclopentadiene intermediate **145**, which is hydrogenated with the aid of the chromium(0) residue and water (Scheme 31) [100–103]. Formation of **145** can be regarded as



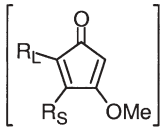
139 **140** **141**

R	(%)	(%)
Bn	24	12
Me	51	0
allyl	18	9

Scheme 30 Formation of 2-(tricarbonylchromiumphenyl)-substituted 1-phenyl-4-azabicyclo[4.1.0]hexanes **140** and their ring-enlargement products **141** from the 1-(*N*-allylamino)-ethylidenetetracarbonylchromium complex **139** [97–99]



142 **58** **143** **144**



145

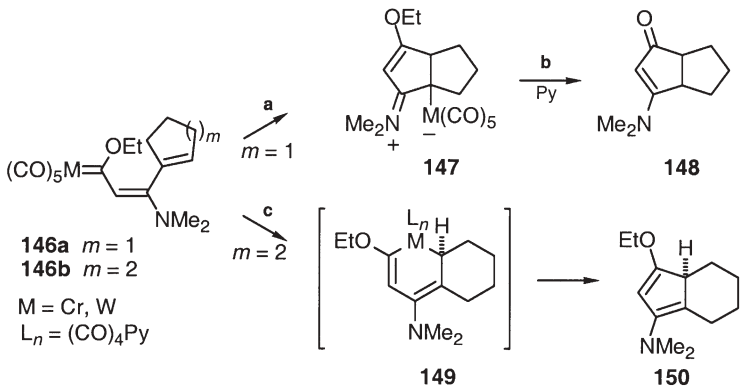
	R_L	R_S	**143** (%)	**144** (%)
a	Ph	Ph	79	4
b	Ph	H	62	0
c	Ph	Me	73	12
d	*n*Pr	*n*Pr	55	0
e	*n*Pr	H	68	0
f	$(CH_2)_4OH$	H	54	0

Scheme 31 Formation of cyclopentenones **143** and **144** by a formal [4+2+1–2] cocyclization from the cyclopropylmethoxycarbenechromium complex **142** and alkynes [100–103]

a formal [4+2+1–2] cocyclization of the complex **142**, an alkyne, and a carbon monoxide molecule with ring opening of the cyclopropyl moiety and loss of an ethene molecule. The cyclopentenone isomers **143** are always obtained as the major products in this reaction, and in most cases the isomers **144** were not observed. In contrast to the chromium complex **142**, its tungsten analog does not give cyclopentenones **143** or **144**, but cycloheptadienone derivatives under the same reaction conditions or even at a higher temperature [104]. It is obvious that ethene is not split off in this case.

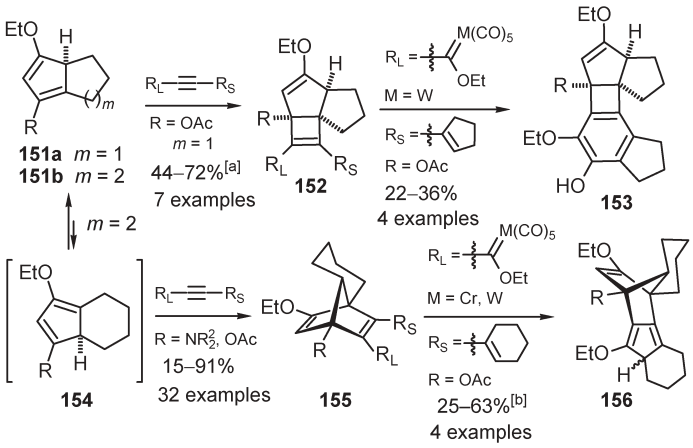
4
Cyclizations and Other Intramolecular Rearrangements of Carbene Complexes

1-Metalla-1,3,5-hexatrienes **146** at ambient temperature undergo a formal 5-*endo-trig*-cyclization to give, after hydrolysis of the enol ether moiety in the corresponding cyclopentadiene, the bicyclo[3.3.0]oct-3-en-2-one **148** (*m*=1) or 7-ethoxy-9-dimethylaminobicyclo[4.3.0]nona-7,9-diene (**150**) (*m*=2) (Scheme 32). Depending on the size of the cycloalkenyl substituent in the 3-position, however, these transformations proceed according to completely different mechanisms. The 3-cyclopentenyl-substituted propenylidenemetal complexes **146a** undergo a rapid intramolecular insertion of the carbon–carbon into the metal–carbene double bond leading to ring-annelated zwitterionic η^1-cyclopenteniminium complexes **147** [105], which are transformed to **148** upon treatment with pyridine and subsequent hydrolysis. On the other hand, complexes **146b** in pyridine prefer to undergo 6π-electrocyclization, probably after loss of one CO ligand, to furnish the pyridine-stabilized chromacyclohexadiene **149** which, by reductive elimination, gives the cyclization product **150** [64, 106, 107]. Even noncoordinating solvents (e.g., toluene) can be used for this cyclization of the cyclohexenyl-substituted complexes **146b**, and none of a zwitterionic intermediate of type **147** could ever be detected.



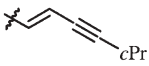
Scheme 32 Two types of cyclization of 3-cycloalkenyl-substituted 1-metalla-1,3,5-hexatrienes **146**. *a*: Et_2O, 20 °C, 12 h, 89%. *b*: Py, C_6D_6, 70 °C, 5 h, 50% conversion. *c*: M=Cr, [D_5]-Py, 20 °C, 18 h, (or 80 °C, 1 h), 100% conversion; M=W, [D_5]-Py, 20 °C, >48 h, 100% conversion [64, 105–107]

Due to the two electron-donating groups in the bicyclic product **150** and the unhydrolyzed precursor of **148**, they should be quite reactive dienes in Diels-Alder reactions. However, such [4+2] cycloadditions were observed only for the cyclohexane-annelated cyclopentadienes **151b**, which equilibrate with the more reactive isomers **154** by 1,5-hydrogen shifts (Scheme 33). The [4+2] cycload-



Scheme 33 [2+2] and [4+2] cycloadditions of cyclopentadienes **151** with alkynes. [*a*] One-pot reaction from the corresponding complex **114** (M=Cr, R=Et, *n*=1) and acetic acid. [*b*] One-pot reaction from the corresponding complex **114** (M=Cr, W, R=Et, *n*=2) and acetic acid [106–110]. For further details see Table 7

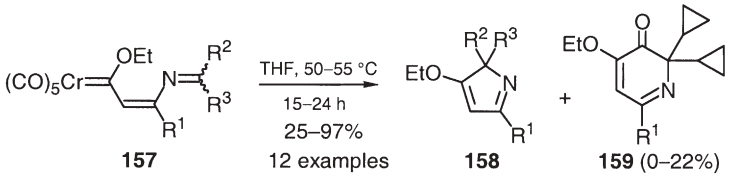
Table 7 [2+2] and [4+2] cycloadditions of cyclopentadienes **151** with alkynes (see Scheme 33)

Entry	R	R_L	R_S	Product	Yield (%)
1	$MeCO_2$	$(CO)_5W{=}C(OEt)$		**152a** **153a**	61 [a] 36[a]+9[b]
2	$BnCO_2$	$(CO)_5W{=}C(OEt)$		**152b** **153b**	72[a] 18[a]+10[b]
3	PhCO	$(CO)_5W{=}C(OEt)$		**152c** **153c**	54[a] 22[a]+20[b]
4	NMe_2	4-CF_3-C_6H_4	H	**155a**	85
5	NMe_2	Ph	H	**155b**	88
6	NMe_2		Ph	**155c**	60
7	NMe_2	4-EtO_2C-C_6H_4	H	**155d**	91
8	NMe_2	1-cyclopentenyl	H	**155e**	43
9	NMe_2	2-isopropenyl	H	**155f**	73
10	NMe_2	2-thienyl	H	**155g**	34
11	NMe_2		*c*Pr	**155h**	46
12	Pyrrolidine	CO_2Et	Ph	**155i**	78
13	OAc	$(CO)_5Cr{=}C(OEt)$		**156**	63 [a,c]

[a] One-pot reaction from the corresponding complexes of type **114** and acetic acid.
[b] The yield of the corresponding hydrolysis product.

ditions of **154** with dienophiles, even with simple alkynes, yield norbornadiene derivatives **155** which, due to through-space interaction between the enol ether moiety and the other carbon–carbon double bond, underwent rapid hydrolysis upon workup and chromatographic purification to yield the corresponding ketones, except for the cases when R_L was a strongly electron-withdrawing group [107, 108]. When cyclopentadiene **154** (R=OAc) was treated with an enynylcarbene complex, the primary adduct **155** underwent a further intramolecular cyclization to yield **156** [109]. In contrast to **151b**, the cyclopentane-annelated cyclopentadienes **151a** prefer to undergo a [2+2] cycloaddition to form tricycles of type **152.** When an enynylcarbene complex is applied as the alkyne in this case, a benzannelation product **153** derived from **152** is eventually formed [110] (Table 7).

An analogous cyclization to eventually form five-membered rings has also been observed for 1-metalla-1,3,5-hexatrienes with an additional heteroatom within the chain, such as in the complexes **157.** These are obtained by Michael additions of imines to alkynylcarbene complexes in good to excellent yields (reaction type F in Scheme 4), and their configurations were determined to be *Z* (≥91%) in all cases. Upon warming in THF solution, complexes **157** underwent cyclization with reductive elimination to furnish 2*H*-pyrroles **158** in up to 97% yield (Scheme 34). With two cyclopropyl substituents at the terminus in



157 **158** **159** (0–22%)

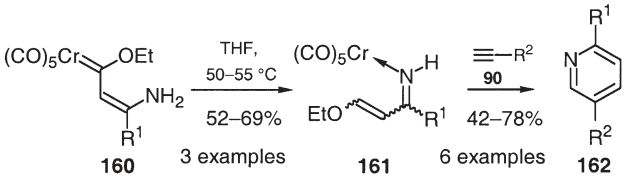
Scheme 34 Cyclizations of 5-hetera-1-metalla-1,3,5-hexatrienes **157** to mainly yield 2*H*-pyrroles [37]. For further details see Table 8

Table 8 Intramolecular cyclization of complexes **157** (see Scheme 34)

Entry	R^1	R^2	R^3	Product	Yield (%)
1	Ph	*p*-$MeOC_6H_4$	*p*-$MeOC_6H_4$	**158a**	25
2	*n*Pr	*p*-$MeOC_6H_4$	*p*-$MeOC_6H_4$	**158b**	57
3	*c*Pr	*p*-$MeOC_6H_4$	*p*-$MeOC_6H_4$	**158c**	65
4	*t*Bu	*p*-$MeOC_6H_4$	*p*-$MeOC_6H_4$	**158d**	78
5	Ph	Ph	*c*Pr	**158e**	62
6	*n*Pr	Ph	*c*Pr	**158f**	88
7	*c*Pr	Ph	*c*Pr	**158g**	97
8	*t*Bu	Ph	*c*Pr	**158h**	85
9	Ph	*c*Pr	*c*Pr	**158i/159i**	45/21
10	*n*Pr	*c*Pr	*c*Pr	**158j/159j**	63/22
11	*c*Pr	*c*Pr	*c*Pr	**158k/159k**	81/0
12	*t*Bu	*c*Pr	*c*Pr	**158l/159l**	92/0

the complex **157** (R^2=R^3=*c*Pr), pyridones **159** were by-products. The formation of the latter must arise after initial carbonyl insertion into the chromium–carbon bond in **157** and a subsequent 6π-electrocyclization. With a cyclopropyl or a *tert*-butyl substituent at the 3-position (R^1=*c*Pr, *t*Bu), the CO-insertion products **159** were not observed. The tungsten complexes of type **157** also yield the products **158**, but require much longer reaction times (7 days) (Table 8).

(2-Aminoalkenyl)carbenechromium complexes **160** with a primary amino group behave quite differently compared to the ones with a secondary or a tertiary amino group (Scheme 35). Upon heating complexes of type **160** in THF, they rearrange to (η^1-1-aza-1,3-butadiene)pentacarbonylchromium complexes **161** which can be isolated in yields of 52–69% [36]. The mechanism of this rearrangement can only be speculated about. It may start with a 1,5-hydride shift, followed by a reductive elimination with a concomitant shift of the pentacarbonylchromium fragment from carbon to nitrogen. In the presence of alkynes **90**, the pentacarbonylchromium-coordinated 1-azabutadienes **161** can undergo a [4+2] cycloaddition and a subsequent 1,4-elimination of ethanol to produce disubstituted pyridines **162**. This rationalization also holds for the formation of pyridines directly from (β-aminoethenyl)carbenechromium complexes **160** and alkynes [88].

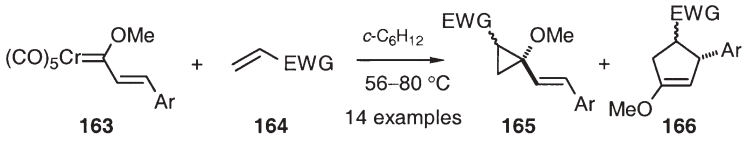


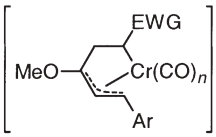
Scheme 35 Formation of 2,5-disubstituted pyridines **162** from α,β-unsaturated complexes with a primary 3-amino group **160** and alkynes **90** [36, 88]

5
Reaction of α,β-Unsaturated Fischer Carbene Complexes with Alkenes, Butadienes, Enamines, and Imines

It is well known that the reaction of Fischer carbene complexes and alkenes with electron-withdrawing substituents affords donor–acceptor-substituted cyclopropanes by a [2+2] cycloaddition with subsequent reductive elimination, rather than the products of an alkene metathesis (cf. Scheme 3) [111–114]. According to Reissig et al., heating of an α,β-unsaturated complex **163** with an electron-deficient alkene **164** not only leads to the expected cyclopropanes **165**, but also to cyclopentenes **166** (Scheme 36) [115, 116] predominantly as the *trans*-isomers with respect to the groups OMe and EWG on the cyclopropane ring in **165** as well as Ar and EWG in **166**. Most probably, the latter products are formed from **165** by a vinylcyclopropane to cyclopentene rearrangement. A systematic study indicated that the yields of cyclopentenes **166** were higher upon longer reaction times, with donor aryl groups (Ar=pyrrolyl) in the 3-po-

sition of **163** and in noncoordinating solvents. Thus, **166** cannot be formed from **165** by a purely thermal vinylcyclopropane rearrangement, but by participation of the chromium fragment via an intermediate of type **167**.



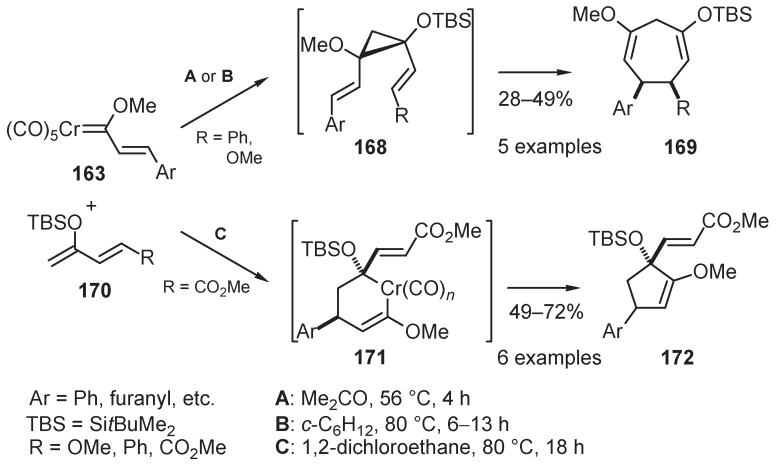


	Ar	EWG	**165** (%)	**166** (%)
a	Ph	CO_2Me	81	–
b	Ph	$CONMe_2$	45	–
c	Ph	CN	59	–
d	Ph	$PO(OMe)_2$	73	–
e		CO_2Me	40	19
f		CO_2Me	–	67

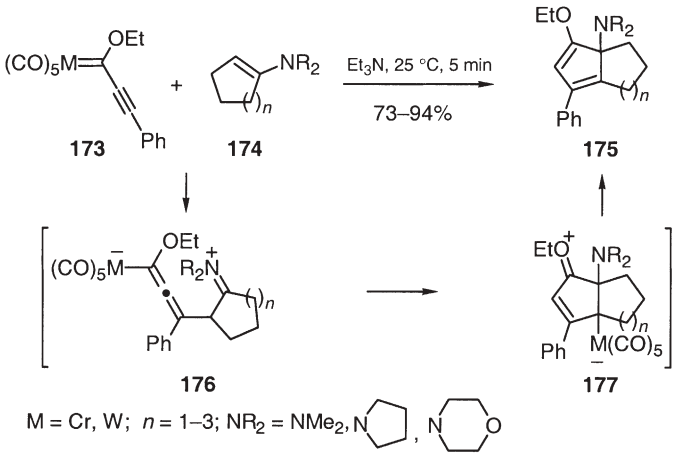
Scheme 36 Synthesis of donor–acceptor-substituted cyclopropanes **165** and cyclopentenes **166** from complexes **163** and acceptor-substituted alkenes **164** [115, 116]

In accordance with this, the reaction of the electron-donor-substituted butadienes **170** (R=Ph, OMe) with the arylcarbene complexes **163** yields divinylcyclopropane intermediates **168** with high chemoselectivity for the electron-rich double bond in **170**, which readily undergo a [3,3]-sigmatropic rearrangement to give the *cis*-6,7-disubstituted 1,4-cycloheptadiene derivatives **169** (Scheme 37) [117, 118]. When the methoxycarbonyl-substituted butadiene **170** (R=CO_2Me) was treated with **163** in the same way, the cyclopentene derivatives **172**, the substitution pattern of which is completely different from that of the cyclopentenes **166**, were obtained. In accordance with the high diastereoselectivity in this reaction, the formation of **172** is attributed to a Diels–Alder reaction of the electron-deficient 1-chroma-1,3-dienes **163** acting as a 4π-component, with the silyloxy-substituted double bond of **170** acting as the 2π-component, yielding the chromacyclohexene intermediate **171**, which then undergoes reductive elimination to furnish **172**.

Another interesting example is provided by the phenylethynylcarbene complex **173** and its reactions with five-, six-, and seven-membered cyclic enamines **174** to form bridgehead-substituted five-, six-, and seven-membered cycloalkane-annelated ethoxycyclopentadienes with high regioselectivity under mild reaction conditions (Scheme 38) [119, 120]. In these transformations the phenylethynylcarbene complex **173** acts as a C_3 building block in a formal [3+2] cycloaddition. Like in the Michael additions (reaction route F in Scheme 4), the cyclic electron-rich enamines **174** as nucleophiles attack the



Scheme 37 Electronic effects of substituents on butadienes **170** determine the formation of cycloheptadienes **169** or cyclopentenes **172** [117, 118]

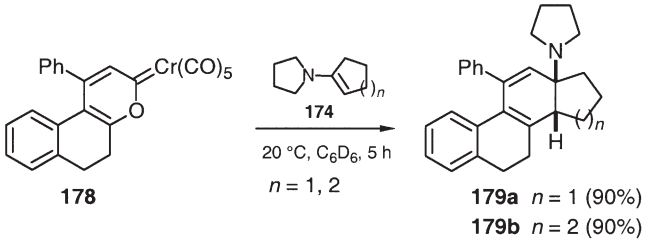


Scheme 38 Formation of five-, six-, and seven-membered cycloalkane-annelated ethoxycyclopentadienes **175** from the phenylethynylcarbene complex **173** and cyclic enamines **174** [119, 120]

electron-deficient triple bond in **173** to give the zwitterionic intermediates **176,** which undergo 1,5-cyclization. Elimination of the pentacarbonylmetal fragment in **177** then furnishes the cyclopentadiene derivatives **175.** This type of ring annelation has been applied to assemble the tetracyclic skeleton of steroids.

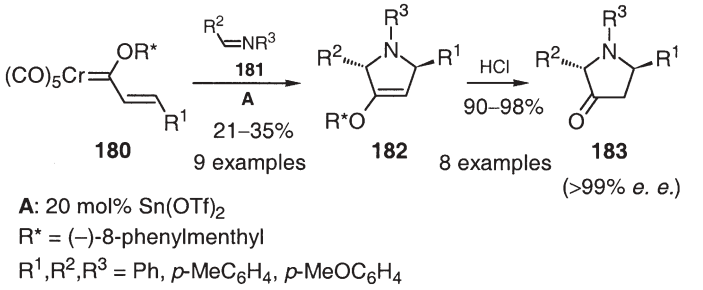
The dihydronaphthalene-annelated pyranylidene complex **178,** prepared according to reaction route E in Scheme 4 from β-tetralone and complex **35,** upon treatment with the pyrrolidinocyclopentene **174** (n=1) or -cyclohexene **174** (n=2) at room temperature gave the tetracyclic compounds **179** in excellent

yields. In this case, the carbenechromium complex **178**, just like α-pyrone, undergoes a [4+2] cycloaddition with the enamine **174** and the cycloadduct fragments to form a cyclohexadiene moiety as well as hexacarbonylchromium (Scheme 39) [29]. *cis*-Elimination of pyrrolidine in the cycloadduct **179a** with the 6-6-6-5 tetracycle is obviously slow, but the 6-6-6-6 tetracyclic analog **179b** eliminates pyrrolidine extremely fast, especially in the presence of silica gel, to yield 11-phenyl-1,2,3,4,5,6-hexahydrochrysene.



Scheme 39 Synthesis of tetracyclic skeletons **179** from the dihydronaphthalene-annelated pyranylidene complex **178** and cyclic enamines **174** [29]

Recently, Akiyama et al. reported an enantiocontrolled [3+2] cycloaddition of chirally modified Fischer alkenylcarbene complexes **180** with aldimines **181** under Lewis-acid catalysis ($Sn(OTf)_2$) to afford enantiomerically pure 1,2,5-trisubstituted 3-alkoxypyrrolines **182** (Scheme 40) [121]. The mode of formation of these products **182** was proposed to be a [4+2] cycloaddition, with the complexes **180** acting as a 1-metalla-1,3-diene with subsequent reductive elimination. Upon hydrolysis under acidic conditions, the enol ethers give the enantiomerically pure 3-pyrrolidinones **183** (Table 9).



Scheme 40 Synthesis of enantiomerically pure 1,2,5-trisubstituted 3-pyrrolidinones **183** from chirally modified 1-alkoxypropenylidene complexes **180** and aldimines [121]. For further details see Table 9

Table 9 Synthesis of enantiomerically pure 1,2,5-trisubstituted 3-pyrrolidinones **183** from chirally modified 1-alkoxypropenylidene complexes **180** and aldimines (see Scheme 40)

Entry	R^1	R^2	R^3	Product	Yield (%)	Product	Yield (%)
1	Ph	Ph	Ph	**182a**	34	**183a**	96
2	Ph	Ph	*p*-MeC_6H_4	**182b**	31	**183b**	91
3	Ph	Ph	*p*-$MeOC_6H_4$	**182c**	30	**183c**	93
4	Ph	*p*-MeC_6H_4	Ph	**182d**	35	**183d**	92
5	Ph	*p*-$MeOC_6H_4$	Ph	**182e**	30	**183e**	90
6	Ph	*p*-ClC_6H_4	Ph	**182f**	27	**183f**	95
7	*p*-ClC_6H_4	Ph	Ph	**182g**	27	**183g**	98

6 Conclusion

In 20 years of usage, α,β-unsaturated Fischer carbene complexes demonstrated their multitalented versatility in organic synthesis, yet new reaction types are still being discovered every year. In view of their facile preparation and multifold reactivity, their versatile chemistry will undoubtedly be further developed and applied in years to come. The application of chirally modified Fischer carbene complexes in asymmetric synthesis has only begun, and it will probably be an important area of research in the near future.

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